

WHAT IS CLAIMED IS:

1. A method for amplification of a population of polynucleotides comprising:
 - (a) reverse transcribing an RNA population to provide a double-stranded cDNA population;
 - 5 (b) digesting said cDNA population with one or more restriction endonucleases having a degenerate recognition or cleavage sequence, wherein said restriction endonuclease is a three- to eight-base cutter and wherein the degenerate recognition or cleavage sequence is represented by the formula of N^m , where N is the extent of degeneracy, and m is the number of degenerate bases, and wherein for at least one of said restriction endonucleases N is 2-4 and m is 1-5, to produce restriction
10 fragments having N^m different single-stranded overhangs for each restriction endonuclease;
 - (c) ligating said restriction fragments to a series of adapters lacking restriction endonuclease sites, each adapter having a sequence complementary to one of said overhangs such that restriction fragments having identical overhangs are ligated to
15 the same adapter; and
 - (d) amplifying said restriction fragments for no more than 25 cycles.
2. The method of claim 1 wherein for at least one of said restriction endonucleases m is 2, 3 or 4.
- 20 3. The method of claim 1 wherein said restriction endonuclease comprises a four-base cutter.
4. The method of claim 1 further comprising digesting the restriction fragments obtained in (b) with one or more further restriction endonucleases producing restriction fragments with single-stranded overhangs different from those produced in (b).
- 25 5. The method of claim 4 further comprising ligating the single-stranded overhangs produced by the digesting of claim 4 to a series of adapters each adaptor having a sequences complementary to one of said overhangs.
6. The method of claim 1 wherein said restriction fragments of (d) are amplified by the polymerase chain reaction (PCR) to produce PCR products.
- 30 7. The method of claim 6 wherein said adapters provide priming sites for said polymerase chain reaction.

8. The method of claim 6 further comprising detecting the PCR products.
9. The method of claim 8 further comprising isolating at least one PCR product.
10. The method of claim 9 further comprising sequencing the at least one isolated PCR product.
- 5 11. The method of claim 9 further comprising cloning the at least one isolated PCR product into a vector.
12. The method of claim 11 further comprising sequencing the cloned PCR product.
13. The method of claim 11 further comprising transforming a recombinant host cell with the vector and expressing the PCR product to produce a polypeptide.
- 10 14. A recombinant host cell transformed with the vector of claim 11.
15. The method of claim 1, wherein said RNA is selected from the group consisting of total RNA, mRNA and enriched poly (A)+ RNA.
16. A method for detecting polymorphism comprising:
- 15 (a) reverse transcribing an RNA population to provide a double-stranded cDNA population;
- (b) digesting said cDNA population with one or more restriction endonucleases having a degenerate recognition or cleavage sequence, wherein the degenerate recognition or cleavage sequence is represented by the formula of N^m , where N is the extent of degeneracy, m is the number of degenerate bases, and m is 1-5, to produce restriction fragments having N^m different single-stranded overhangs for each restriction endonuclease;
- 20 (c) ligating said restriction fragments to a series of adapters lacking restriction endonuclease sites, each adapter having a sequence complementary to one of said overhangs such that restriction fragments having identical overhangs are ligated to the same adapter;
- 25 (d) amplifying said restriction fragments for no more than 25 cycles;
- (e) sequencing the amplified restriction fragments, and
- (f) comparing the sequence of the amplified restriction fragments with the sequence of the same restriction fragments from a reference source.
- 30 17. The method of claim 16 wherein said RNA is selected from the group consisting of total RNA, mRNA and enriched poly (A)+ RNA

18. A method for detecting a change in the pattern or amount of RNA expression in a tissue or cell associated with an internal or external factor comprising:

(1) determining the pattern of RNA expression in a first tissue or cell sample not subject to the internal or external change by a method

5 comprising

(a) reverse transcribing an RNA population to provide double-stranded cDNA;

10 (b) digesting said double-stranded cDNA prepared from said first sample with one or more restriction endonucleases having a degenerate recognition or cleavage sequence, wherein the degenerate recognition or cleavage sequence is represented by the formula of N^m , where N is the extent of degeneracy, m is the number of degenerate bases, and m is 1-5, to produce restriction fragments having N^m different single-stranded overhangs for each restriction endonuclease;

15 (c) ligating said restriction fragments to a series of adapters lacking restriction endonuclease sites, each adapter having a sequence complementary to one of said overhangs such that restriction fragments having identical overhangs are ligated to the same adapter;

(d) amplifying said restriction fragments for no more than 25 cycles; and

20 (e) determining the pattern of RNA expression in said first sample;

(2) determining the pattern or amount of RNA expression in a second tissue or cell subject to the internal or external factor by performing the steps (1)(a)-(e) with said second tissue or cell; and

25 (3) comparing said first and said second patterns or amounts to determine the effect of the internal or external factor on the pattern of RNA expression in the tissue or cell.

19. The method of claim 18 wherein said internal or external factor is a disease, condition or disorder.

30 20. The method of claim 18 wherein said first tissue or cell and said second tissue or cell are in different stages of development.

21. The method of claim 18 wherein said tissue or cell comprises a plant tissue or cell.

22. A method for diagnosis of a disease, condition or disorder comprising:

5 (1) determining the pattern or amount of RNA expression in a first tissue or cell obtained from an organism free of said disease, condition or disorder by a method comprising

(a) reverse transcribing an RNA population to provide double-stranded cDNA;

10 (b) digesting said double-stranded cDNA prepared from said first sample with one or more restriction endonucleases having a degenerate recognition or cleavage sequence, wherein the degenerate recognition or cleavage sequence is represented by the formula of N^m , where N is the extent of degeneracy, and m is the number of degenerate bases, and wherein m is 1-5, to produce restriction fragments having N^m different single-stranded overhangs for each restriction endonuclease;

15 (c) ligating said restriction fragments to a series of adapters lacking restriction endonuclease sites, each adapter having a sequence complementary to one of said overhangs such that restriction fragments having identical overhangs are ligated to the same adapter;

20 (d) amplifying said restriction fragments for no more than 25 cycles; and

(e) determining the pattern of RNA expression in said first sample;

25 (2) determining the pattern or amount of RNA expression in a second tissue or cell obtained from an organism having said disease, condition or disorder by performing the steps (1)(a)-(e) with said second tissue or cell;

(3) comparing said first and said second patterns or amounts to determine the effect of said disease, condition or disorder on the pattern or amount of RNA expression in the tissue or cell; and

30 (4) if said disease, condition or disorder results in a change in the pattern or amount of RNA expression, using said change as an indication of the presence of said

disease, condition or disorder, and the absence of said change as an indication of the absence of said disease, condition, or disorder.

tissue or cell.

23. An isolated nucleic acid molecule comprising an oligonucleotide
5 selected from the group consisting of: SEQ ID NOs: 2-65.